# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference TIE-001-PCT-PRIO1 | **FOR FURTHER ACTION** | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
|---|---|---|
| International application No. PCT/EP2003/009393 | International filing date *(day/month/year)* 25.08.2003 | Priority date *(day/month/year)* 25.08.2003 |
| International Patent Classification (IPC) or both national classification and IPC G01N33/543 | | |
| Applicant RAMAEL, Marc, et al. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 8 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 25.03.2005 | 23.12.2005 |
| Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | Authorized Officer Luis Alves, D Telephone No. +49 89 2399-8695 |

**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

International application No. PCT/EP2003/009393

**I. Basis of the report**

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

**Description, Pages**

1-66 as originally filed

**Claims, Numbers**

1-33 received on 12.12.2005 with letter of 09.12.2005

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 13, 30 (both partially)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. as above

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Yes: | Claims | 1-33 |
| | No: | Claims | |
| Inventive step (IS) | Yes: | Claims | 1-33 |
| | No: | Claims | |
| Industrial applicability (IA) | Yes: | Claims | 1-33 |
| | No: | Claims | |

2. Citations and explanations

**see separate sheet**

**Section III:**

1. The subject-matter of claims 13 and 30 has only partially been searched (see International Search Report). Consequently, no opinion will be established on subject-matter encompassed by said claims but which has not been searched (Rule 66.1( e) PCT)

**Section V:**

The following document, cited in the International search report, is referred to in this International Preliminary Examination Report:

D1: TORCHILIN V P ET AL: "ANTIBODY-LINKED CHELATING POLYMERS FOR IMMUNOIMAGING IN VIVO" JOURNAL OF CONTROLLED RELEASE, ELSEVIER SCIENCE PUBLISHERS B.V. AMSTERDAM, NL, vol. 11, 1989, pages 297-303.

1. D1 discloses antibody-linked chelating polymers for immunoimaging, in particular (see abstract) dextran derivatives comprising antibodies to analyte. This derivative may be further modified with biotin (which is bound either to dextran or antibody).
D1 also discloses antibody-polymer conjugates wherein the polymer possesses large numbers of metal binding sites (see p.297, left-hand column, second sentence) and p.300, right-hand column, last sentence to p.301, left-hand column, first sentence).
Secondary labelled antibody is added after the conjugate is added to the sample.

Present claim 1 is distinguished therefrom by the following features: Addition of antibody against the tag on the analyte, the antibody having a metal particle label of average diameter between 0.6 and 40 nm; Addition of antibody conjugate comprising one or

more anti-A antibodies directed against immunoglobulins of species A and one or more anti-B antibodies directed against immunoglobulins of species B; A metal enhancement step.
Therefore, the subject-matter of claim 1 complies with the requirements of Article 33(2) PCT.

The technical problem to be solved by present claim 1 with respect to the method disclosed in D1 is the provision of a sensitive in vitro method with reduced background signal.

The solution defined in claim 1 is not suggest in any of the available documents taken alone or in combination. Therefore, the subject-matter of claim 1 seems to comply with the requirements of Article 33(3) PCT.
The same reasoning applies to independent claims 2 to 5 and 23 to 26; which also comprise the features use of a metal particle label of average diameter between 0.6 and 40 nm; Addition of antibody conjugate comprising one or more anti-A antibodies directed against immunoglobulins of species A and one or more anti-B antibodies directed against immunoglobulins of species B; A metal enhancement step.

Claims 6 to 9, 27 and 31 to 33 refer back to said independent claims and therefore also comply with the requirements of Article 33(2) and (3) PCT.

None of the available prior art documents discloses a conjugate comprising one or more antibodies against immunoglobulins of species A, one or more antibodies against immunoglobulins of species B and metal particles of average diameter between 0.6 and 40 nm. Therefore, the subject-matter of claims 10 to 22 to 28 to 30 is novel (Article 33(2) PCT).
For the same reasoning as above the solution defined in independent claims 10 and 28 seems to involve an inventive step. Therefore, the subject-matter of claims 10 and 28, and dependent claims 11 to 22, 29 and 30 appears to comply with the requirements of Article 33(3) PCT.

2. The subject-matter of claims 1 to 33 is industrially applicable.